American Journal of Hematology 58:326–329 (1998)

Invasive Pulmonary Mucormycosis With Rupture of the Thoracic Aorta

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We report an acute myelogenous leukemia patient with mucormycosis who died of massive hemoptysis during antifungal therapy. The diagnosis was made postmortem and autopsy revealed that the pulmonary nodule consisting of mucorales protruded over the luminal surface of the aorta. Microscopic examination showed the invasion of mucor hyphae into the wall of the aortic arch. Surgical treatment may be indicated for patients with pulmonary mucormycosis refractory to amphotericin B therapy. Am. J. Hematol. 58:326–329, 1998. © 1998 Wiley-Liss, Inc.

Key words: acute myelogenous leukemia; mucormycosis; hemoptysis

INTRODUCTION

Mucormycosis (zygomycosis) is a rare opportunistic fungal infection caused by mucorales that belong to the genera Mucor, Rhizopus, and Absidia [1–3]. The infection develops in patients with hematological malignancies being treated with antibacterial drugs or cytotoxic agents [4,5]. Since the zygomycetes have a predilection for blood vessels, thrombus formation and infarction are the common characteristic findings.

Recently, we have encountered two cases of mucormycosis associated with hematological malignancies. One patient had refractory anemia, and the other acute myelogenous leukemia. At autopsy of the former patient, mucor was found in the thrombus in the ventricle of the heart. In this article, we report the latter case of mucormycosis associated with acute myelogenous leukemia. The patient died of massive hemoptysis resulting from mucor invasion of the aorta. To our knowledge, this is the first report of pulmonary mucormycosis with fatal bleeding from the aorta.

CASE REPORT

A 63-year-old man was hospitalized because of general fatigue in October 1995, and diagnosed with acute myelogenous leukemia, M2 subtype according to the FAB classification.

Remission induction therapy with behenoyl cytarabine, daunorubicin, 6-MP, and prednisolone was started on November 26, 1995. Seven days after chemotherapy, the patient developed high-grade fever with severe leukopenia (800/μl), and antibiotics and fluconazole (400 mg/day) were begun. However, high-grade fever persisted, and hoarseness due to recurrent nerve paralysis was recognized. Chest X rays showed a large consolidation shadow adjacent to the aortic arch in the left upper lobe and a round lesion in the right upper lobe (Fig. 1A and B). Because fungal infection was strongly suspected, continuous infusion of amphotericin B (0.5 mg/kg/day) was started. Thereafter, the patient became afebrile and C-reactive protein levels decreased. A month later, a ''fungal ball''-like shadow was recognized in the right upper lobe (Fig. 1C). Pleural effusion was seen, but mucor could not be detected in the culture of pleural fluid. During this period, sputum and blood culture were negative for zygomycetes.

A cumulative dose of 2.7 g amphotericin B was administered over 3 months. However, there was no significant improvement of pulmonary infiltrates on chest X

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Received for publication 28 May 1997; Accepted 8 April 1998

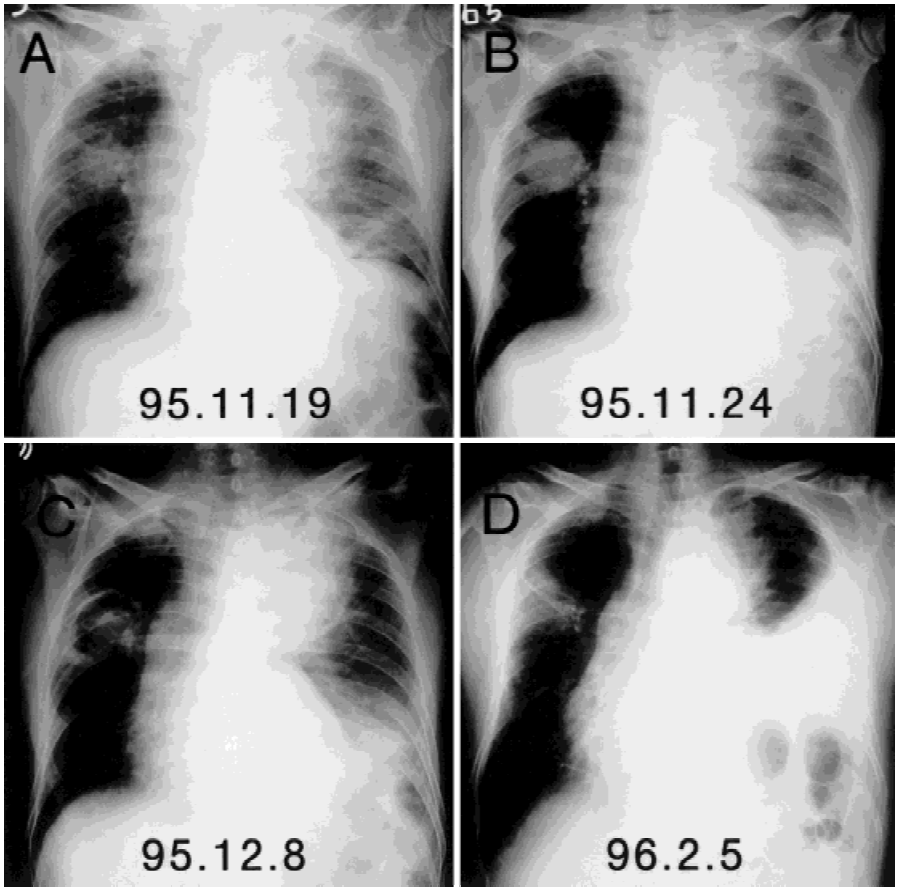

Fig. 1. Chest X-ray film showing consolidation shadow adjacent to the aortic arch in the left upper lobe and a round lesion in the right upper lobe (A and B). A ''fungal ball''-like shadow is in the right upper lobe (C). Pleural effusion is in the left lung (D).

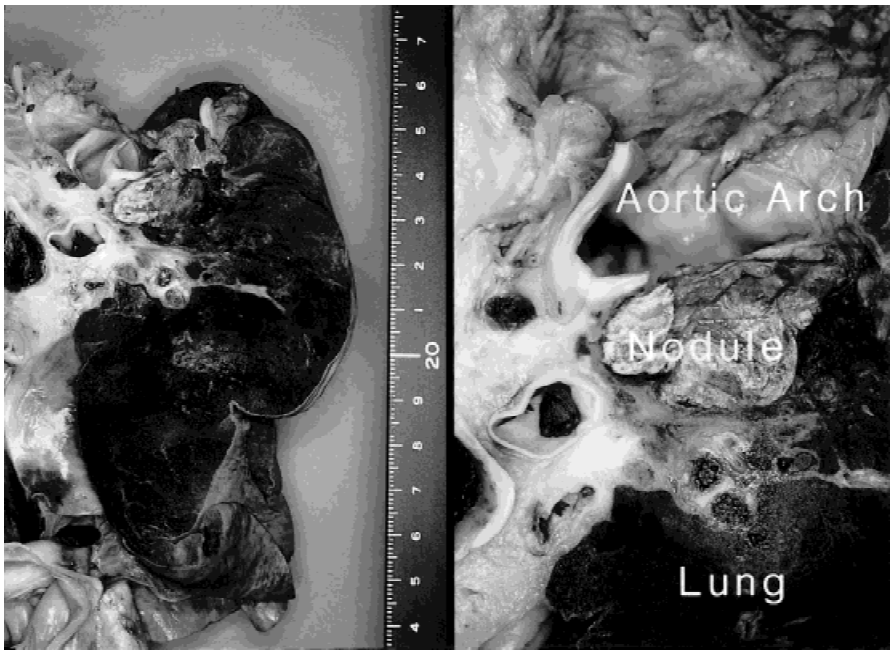

Fig. 2. Autopsy finding. A round nodule that projected into the aortic arch at the left upper lobe.

rays (Fig. 1D). Amphotericin B treatment was replaced by oral itraconazole therapy (200 mg/day). Maintenance therapy with oral cytarabine ocfosfate was begun. Bronchoscopy was performed in February 1996, and transbronchial lung biopsy showed granulation tissue, but there was no evidence of fungal infection. Culture of the bronchoalveolar lavage fluid was positive for Pseudomonas aeruginosa and Candida krusei, but negative for zy-

gomycetes. He remained in remission and appeared well at the outpatient clinic over the next 4 months during which he was treated with oral cytarabine ocfosfate and itraconazole. On August 13, 1996, the patient suddenly developed massive hermoptysis and was hospitalized. On August 17, he died of asphyxia.

At autopsy, a round nodule measuring about 2 × 3 cm was found in the left upper pulmonary lobe, and projected into the aortic arch (Fig. 2). Microsection of the nodule showed central necrosis. Inflammatory cells infiltrated into the wall of the aortic arch, and degeneration of the elastic fiber of the vessel was seen. The artery that fed the aortic arch was occluded by thrombus (Fig. 3A), in which non-septate hyphae of mucor were detected (Fig. 3B). The cause of death was considered hemorrhage resulting from the invasion of mucor into the aortic arch.

DISCUSSION

One of the major risk factors of fungal infection is leukopenia in patients undergoing cytotoxic chemotherapy for leukemia and lymphoma. Although compared to candidasis and aspergillosis, mucormycosis is a rare fungal infection, it has shown an increasing incidence and is receiving more attention from physicians [6].

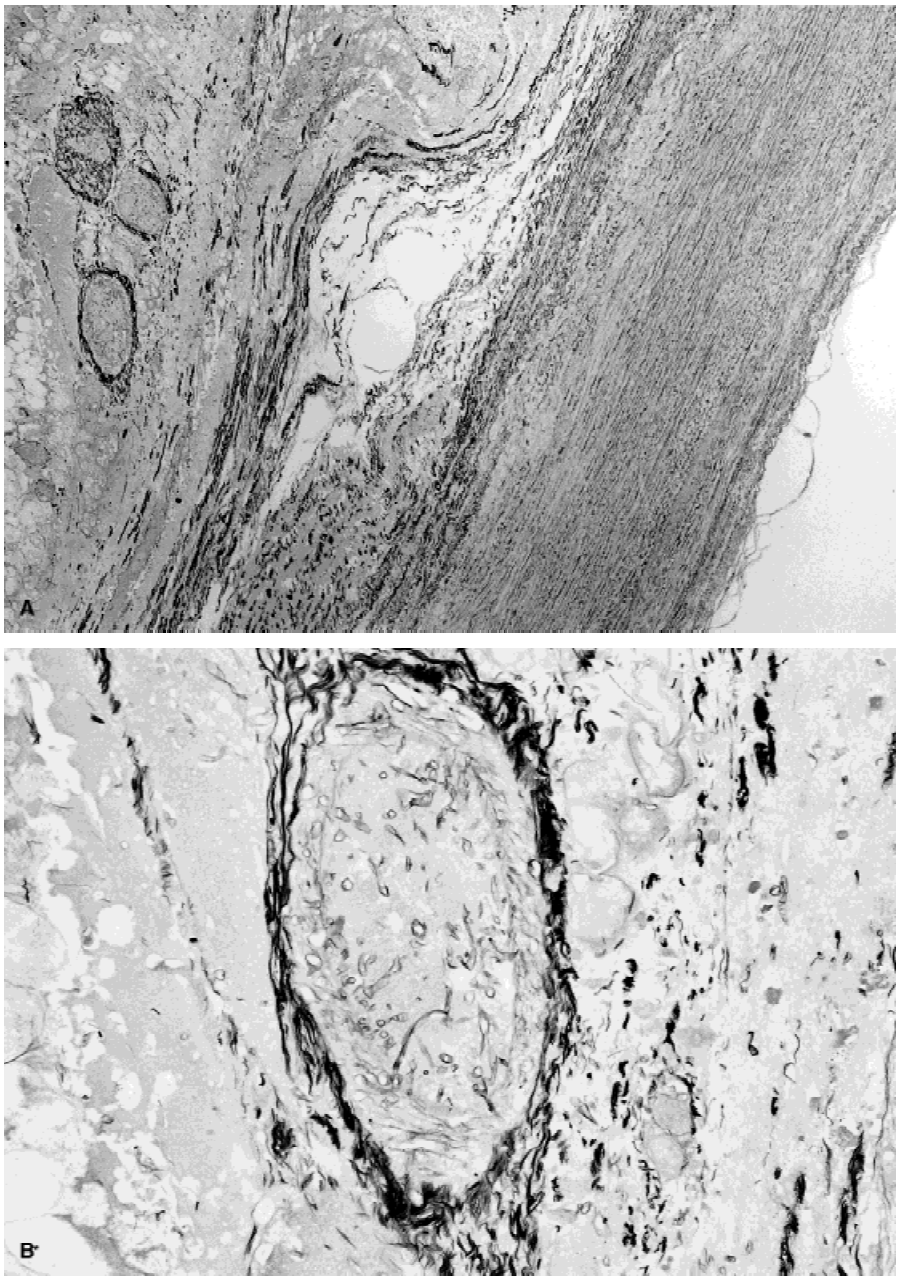

Fig. 3. Microscopic findings. A: Non-septate hyphae of mucor were noted in the thrombus in the artery that fed the aortic arch. B: Hyphae projected into the aortic arch was occluded by thrombus.

The clinical form of mucormycosis is categorized as cutaneous, rhinocerebral, gastrointestinal, pulmonary, and widely disseminated forms. In immunocompromised hosts, the disease tends to occur in the lungs and widely disseminate. Mucormycosis as well as aspergillosis has a predilection for arteries, causing thrombus formation and infarction of organs. Accordingly, mucormycosis is often fatal and prognosis of mucormycosis is worse than that of aspergillosis, although there has been a few reports of successful treatment for mucormycosis [1].

The diagnosis of mucormycosis is difficult, because tissue culture may be negative and there is no serological test for mucor [2,3]. A definitive diagnosis depends on the identification of mucoraceus hyphae in tissues. Despite transbronchial lung biopsy, we could not have a definite diagnosis.

The only effective antifungal agent is amphotericin B. Azole derivatives and flucytosine have little activity against mucor [2,3,7,8]. In our case, the symptoms were alleviated by continuous infusion of amphotericin B with a daily dose of 0.5 mg/kg. The appearance of high-grade fever and pulmonary infiltrates despite administration of antibiotics and antifungal agents (azole derivatives) suggests mucormycosis, and earlier biopsy may be lead to earlier diagnosis and thus to successful treatment with infusion of amphotericin B. We would like to emphasize that suspicion of mucormycosis is critical for successful treatment of mucorycosis. There have been a few reports describing successful treatment of mucormycosis with pulmonary lobectomy [9]. Surgical debridement should have been considered in the present case.

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